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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/785,455	01/17/97	HODGSON	J . . P31353

EXAMINER	
HOBBS, L	
ART UNIT	PAPER NUMBER
1814	6

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DATE MAILED: 10/27/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 6/25/97

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-27 is/are pending in the application.
Of the above, claim(s) 13-25 + 27 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-3, 7-12 + 26 is/are rejected.
☒ Claim(s) 4-6 is/are objected to.
☒ Claim(s) 1-27 are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948. substitute
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: 9601095.4 (1/19/96) 9615845.6 (1/27/96)

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948 substitute
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-421-632/40206

DETAILED ACTION

1. This application has been filed with informal drawings which are acceptable for examination purposes only, please refer to the attached substitute PTO-948 form for details. Formal drawings will be required when the application is allowed.

2. Acknowledgment is made of applicant's claim for priority based on two applications filed in the United Kingdom: 9601095.4, filed January 19, 1996, and 9615845.6, filed January 27, 1996. It is noted, however, that applicant has not filed certified copies of the applications as required by 35 U.S.C. § 119.

3. The title of this application has been changed to "DNA Encoding Methionyl tRNA Synthetase from Staphylococcus aureus".

4. Claims 1-12 and 26 are pending in this application. Claims 13-25 and 27 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

Election/Restriction

5. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-12 and 26, drawn to DNA molecules encoding methionyl tRNA

synthetase (MetRS), vectors host cells and recombinant methods of production, classified in class 435, subclass 183.

II. Claims 13 and 14, drawn to MetRS protein, classified in class 435, subclass 183.

III. Claims 15 and 23-25, drawn to antibodies, immunological compositions and methods of inducing immunological responses, classified in class 424, subclass 130.1.

IV. Claims 16 and 19, drawn to antagonists and methods of treatment using antagonists, classified in class 514, subclass 12.

V. Claim 18, drawn to gene therapy, classified in class 514, subclass 44.

VI. Claim 20, drawn to diagnosis using DNA molecules, classified in class 435, subclass 6.

VII. Claims 17, 21, 22 and 27, drawn to methods involving MetRS, classified in class 424, subclass 94.5.

The inventions are distinct, each from the other because of the following reasons:

6. Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process

(MPEP § 806.05(f)). In the instant case, the DNA molecules of Group I may be used for hybridization probes, as opposed to making the enzyme of Group II, and the enzyme of Group II may be produced by isolation from natural sources or by synthesis, as opposed to the recombinant methods of Group I.

7. Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the DNA molecules of Group I may be used for hybridization methods, as opposed to the genetically based immunological methods of Group III.

8. Invention I is patentably distinct from Inventions IV and VII. The DNA molecules of Group I are not required for the treatment methods using an antagonist of the enzyme, Group IV, or methods using the enzyme itself, Group VII; the Groups each have separate utilities, such as use of the Group I DNA molecules for hybridization methods, versus use of the Group IV methods to treat patients requiring *S.aureus* MetRS inhibition, versus the use of the enzyme methods to diagnose or treat patients requiring *S.aureus* MetRS; are physically, chemically and biologically different from each other;

and are subject to separate manufacture and sale from each other. These groups have acquired separate status in the art and separate fields of search as further evidenced by their separate classification.

9. Inventions I and V are related as product and process of use. See MPEP § 806.05(h). In the instant case, the DNA molecules of Group I may be used for hybridization methods, as opposed to the gene therapy methods of Group V.

10. Invention I and VI are patentably distinct from each other. The DNA molecules of Group I are not required for the practice of the diagnosis methods of Group VI; the Groups each have separate utilities, such as use of the Group I DNA molecules for recombinant production of enzyme, versus use of the Group VI methods to diagnose patients; are physically, chemically and biologically different from each other; and are subject to separate manufacture and sale from each other. These groups have acquired separate status in the art and separate fields of search as further evidenced by their separate classification.

11. Inventions II and III are related as product and process of use. See MPEP § 806.05(h). In the instant case, the enzyme of Group II may be used for its enzymatic activities, as opposed to the immunological methods of Group III.

12. Inventions II and IV are patentably distinct from each other. The enzyme of Group II is not required for the treatment methods using an antagonist of the enzyme, Group IV; the Groups each have separate utilities, such as use of the Group II enzyme for creating antibodies, versus use of the Group IV methods to treat patients requiring *S.aureus* MetRS inhibition; are physically, chemically and biologically different from each other; and are subject to separate manufacture and sale from each other. These groups have acquired separate status in the art and separate fields of search as further evidenced by their separate classification.

13. Inventions II and V are related as process of making and product made. See MPEP § 806.05(f). In the instant case, the enzyme can be isolated the *in vivo* genetic therapy methods of Group V.

14. Inventions II and VI are patentably distinct from each other. The enzyme of Group II is not required for the methods of diagnosis using nucleic acid sequencing, Group VI; the Groups each have separate utilities, such as use of the Group II enzyme for creating antibodies, versus use of the Group VI methods to diagnose patients; are physically, chemically and biologically different from each other; and are subject to separate manufacture and sale from each other. These groups have acquired separate

status in the art and separate fields of search as further evidenced by their separate classification.

15. Inventions II and VII are related as product and process of use. See MPEP § 806.05(h). In the instant case, the enzyme of Group II can be used for creating antibodies, as opposed to the methods of Group VII.

16. Inventions III and IV are related as product and process of use. See MPEP § 806.05(h). In the instant case, the antibodies of Group III can be used for *in vitro* assays for the presence of the enzyme, as opposed to the patient treatment methods of Group IV.

17. Inventions III, V and VI are patentably distinct from each other. The immunological methods of Group III are not used in the treatment methods of Group V, or the diagnosis methods of Group VI, and each of the methods of Groups V and VI are not required for the practice of the other Group; the Groups each have separate utilities, such as use of the Group III methods to create antibodies, the use of Group V methods to treat patients and the use of the Group VI methods for diagnosis of *S.aureus* infection; are physically, chemically and biologically different from each other; and are subject to separate manufacture and sale from each other. These groups have acquired

separate status in the art and separate fields of search as further evidenced by their separate classification.

18. Inventions III and VII are related as product and process of use. See MPEP § 806.05(h). In the instant case, the antibodies of Group III can be used as antagonists for patient treatment methods, as opposed to the *in vitro* assays of Group VII.

19. Inventions IV, V and VI are patentably distinct from each other. The treatment methods using an antagonist of the enzyme, Group IV, are not used in the gene therapy methods of Group V, or the diagnosis methods of Group VI, and each of the methods of Groups V and VI are not required for the practice of the other Group; the Groups each have separate utilities, such as use of the Group IV methods to treat patients requiring S.aureus MetRS inhibition, the use of Group V methods in gene therapy and the use of the Group VI methods for diagnosis of *S.aureus* infection; are physically, chemically and biologically different from each other; and are subject to separate manufacture and sale from each other. These groups have acquired separate status in the art and separate fields of search as further evidenced by their separate classification.

20. Inventions IV and VII are related as product and process of use. See MPEP § 806.05(h). In the instant case, the antagonists of Group III can be used for patient

treatment methods, as opposed to the *in vitro* assays of Group VII.

21. Inventions V and VII are patentably distinct from each other. The methods of Group V are not required for the practice of the methods of Group VII; the Groups are physically, chemically and biologically different from each other; and are subject to separate manufacture and sale from each other. These groups have acquired separate status in the art and separate fields of search as further evidenced by their separate classification.

22. Inventions VI and VII are patentably distinct from each other. The methods of Group VI are not required for the practice of the methods of Group VII; the Groups each have separate utilities, such as use of the Group VI methods to diagnose patients and the use of the Group VII methods for assays; are physically, chemically and biologically different from each other; and are subject to separate manufacture and sale from each other. These groups have acquired separate status in the art and separate fields of search as further evidenced by their separate classification.

23. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and their recognized divergent subject matter, and the search required for any one of the Groups

is not required for any other, restriction for examination purposes as indicated is proper.

24. During a telephone conversation with Edward R. Gimmi on October 7, 1997 a provisional election was made without traverse to prosecute the invention of group I, claims 1-12 and 26. Affirmation of this election must be made by applicant in responding to this Office action. Claims 13-25 and 27 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention.

25. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

26. Claim 1, with depending claims 2, 3 and 8-11, claim 7, claim 12, and claim 26 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the sequences, and their complements, as disclosed in the

specification, not to any sequence: (1) with 70% or more homology to the disclosed sequences (claims 1 and 7); (2) which has any 15 consecutive nucleotides of the disclosed sequences (claim 1); (3) which has any 15 nucleotides, not even consecutive, of the polynucleotides (claim 7); (4) which is any "fragment" of the disclosed sequences (claims 1, 7, 12 and 26), including any "fragment" which hybridizes under "stringent conditions" (claim 26). See M.P.E.P. §§ 706.03(n) and 706.03(z). The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of DNA fragments, some encoding binding and/or enzymatic activity, naturally occurring or synthetic, encompassed.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands, 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir., 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

These claims are drawn to encompass DNA fragments which encode all, a portion, or even a very small part of a MetRS from *S.aureus*. The specification, however, only discloses Seq. ID Nos.: 1 and 2. Despite knowledge in the art for the production of nucleotide sequences encoding peptide fragments, the specification fails

to provide guidance regarding how to make and use all of the possible fragments or structures with 70%, or more, homology, any 15 consecutive nucleotides, any 15 nucleotides, or any fragment or portion of the disclosed sequences, only some of which would retain a stated activity.

The amino acid sequence of a protein determines its structural and functional properties, and predictability of which amino acids can be changed or removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of this protein is lacking, it is unpredictable as to which peptide fragments, if any, meet the limitations of the claims. Furthermore, while recombinant techniques are available, it is not routine in the art to screen large numbers of DNA molecules encoding peptide fragments with oligonucleotides which may or may not be specific to the desired enzyme and where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. Therefore, one of ordinary skill would require guidance, such as information regarding the extent of peptide fragmentation, the location of fragmentation sites, and the specific amino acid changes which would result in the preservation of the stated activity, and be 70%, or more, homologous, as well as which oligonucleotide fragments, of 15 nucleotides or more, are specific to the enzyme of

interest, in order to make and use DNA fragments, portions and sequences with 70%, or more, homology, and 15mer oligonucleotides in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

27. Claims 4-6 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

28. Claim 26 is rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for polynucleotides encoding MetRS, does not reasonably provide enablement for such polynucleotides "obtainable" from a DNA library. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands, 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir., 1988), *supra.*

While the specification discloses polynucleotides encoding MetRS, claim 26 is not properly enabled by this disclosure because the claim contains the phrase "obtainable". The assessment and summation of the potential "obtainability" of an

agent such as a nucleic acid is not a reasonably determinable quality. It is subjective and is not constant in all instances; simply put, a chemical compound, such as a polynucleotide, either is or is not obtained by screening an appropriate library. Thus a DNA molecule is either obtained or it is not obtained by screening because there are no known examples of DNA molecules which are conditionally present per se.

The Examiner notes that alteration of the claims to positively recite "obtained" would obviate this rejection.

29. Claim 26 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims encompass isolated DNA molecules "...consisting essentially of..." other DNA sequences. The phrase "...consisting essentially of..." is a transition phrase used in claims drawn to a composition for partially limiting the scope of the claims to specified elements and those that do not materially affect the basic and novel characteristics of the composition. Since isolated DNA molecules are not compositions, they can only comprise (open to the presence of other elements), or in the alternative, consist of (closed to all other elements) other sequences. The use of a partially limiting transition phrase renders claims to isolated DNA molecules indefinite. As a result, the claims have been interpreted, and treated on their merits, by the examiner as if "comprising" was the transition term used.

Alteration of the claim language to either "comprising" or "consisting of" would be an appropriate correction.

30. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 7 and 8 are rejected under 35 U.S.C. 102(a) as being anticipated by Bult et al. [(1996) Science 273(5278): 1058-1073 and Genbank submission U67567/ L77117, made on August 20, 1996]. Bult et al. teach a DNA molecule comprising at least 15 sequential bases of a polynucleotide encoding Seq. ID No.: 2 (see attached sequence listing). The also teach the placement of the DNA molecule into a vector system as part of a library (p. 1058, col. 3).

31. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable

over Bult et al. and Georgiou [(1988) AIChE J. 34(8): 1233-1248]. Bult et al., as discussed previously, teach a DNA molecule, and thus its corresponding RNA, comprising at least 15 sequential bases of a polynucleotide encoding Seq, ID No.: 2 (see attached sequence listing). The also teach the placement of the DNA molecule into a vector system as part of a library (p. 1058, col. 3). Georgiou teaches the placement of genes of interest into vectors, with various promoters, then transforming the vectors into host cells for the purposes of recombinant expression of the proteins of interest from the DNA molecules.

It would have been obvious to one of ordinary skill in the art, at the time the invention was made, to combine the teachings of Bult et al., a polynucleotide encoding MetRS from *Methanococcus jannaschii*, with the teachings of Georgiou, placing DNA molecules into selected vectors, transforming host cells and subsequent expression of the polypeptides in order to express the MetRS of *M.jannaschii*. One would have a reasonable expectation of success since the gene is homologous to other, previously expressed, MetRS genes and Georgiou teaches systems which express various proteins of interest (Table 1).

32. Claims 4-6 and 26 are allowable over the prior art of record.

33. This application currently names joint inventors. In considering patentability of

the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

34. Any inquiry concerning this communication or earlier communications should be directed to Lisa J. Hobbs whose telephone number is (703) 308-6573.

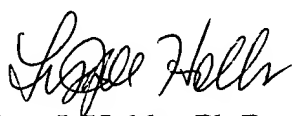
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at (703) 308-4216.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission to the attention of the examiner in Art Unit 1814. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (October 19, 1988) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The FAX telephone number is (703) 308-4242. Note: If applicants do submit a paper by facsimile, the original signed copy should be retained by applicants or applicants' representative. No duplicate copies should be submitted so as to avoid the processing of duplicate papers in the Office.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**robert.wax@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified and/or exchanged unless there is of record an express waiver of the confidentiality requirements of 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published in the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.



Lisa J. Hobbs, Ph.D.
October 23, 1997